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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/784,332	02/16/2001	Gregory Plowman	038602-1083	2179

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EXAMINER	
MONSHIPOURI, MARYAM	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 05/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/784,332	PLOWMAN ET AL.	
	Examiner	Art Unit	
	Maryam Monshipouri	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-18, 21-25, 28-29 and 31* is/are pending in the application.

4a) Of the above claim(s) *17,18 and 28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-25, 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claims 1-16, 19-20, 26-27and 30 have been canceled. Claims 21-25 and 29 and 31 are still at issue and are present for examination. Claims 17-18 and 28 are withdrawn as drawn to non-elected invention.

Applicants' arguments filed on 3/3/2004, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 24 and 31 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, as stated in the previous office action. In traversal of this rejection applicant argues that the Office has viewed the term "modulates" too narrowly. Applicant refers to page 16 of the specification and states that in said page the term "modulates" refers to the ability of a compound to alter the function of AUR1 and/or AUR2 and said alteration is directed to the function of AUR1 and/or AUR2 by increasing or decreasing the probability that a complex forms between AUR1 and AUR2 and a natural binding partner. According to applicant, these definition do not require direct interaction of a modulator with an Aurora polypeptide.

Applicant continues by stating that antisense DNA indirectly modulate Aurora protein activity by reducing the amount of said protein in cells. The amount of protein impacts the portein's function in a cell and also affects whether a complex forms between the protein and its binding partner. Hence, according to applicant, said claims are not indefinite and the rejection should be withdrawn.

These arguments were fully considered but were found **unpersuasive**. This is because applicant has misunderstood in assuming that the Office has viewed the term "modulates" too narrowly. In drafting said rejection the Office viewed the term "modulates" as applying to all compounds that alter the activity of AUR1-2 polypeptides **both directly and indirectly**.

However, as mentioned previously, applicant is reminded that elected claims are directed to methods of use of modulators of (kinase) activity of AUR 1-2 polypeptides and not modulators of DNA expressing said polypeptides. Therefore, it still remains unclear how antisense can be a modulator of said polypeptides. Applicant is well aware that antisense is only capable of affecting the amount of protein through interacting with DNA, decreasing its expression etc. and hence, can only be interpreted as an indirect or direct modulator of DNA. If applicant intends to claim a method of use of modulators of broader scope he/she must amend claim 21 to refer to method of use of modulators of both DNA and polypeptides.

Claims 22-23, 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 22-23 and 29 (which depend from claim 21)

recite the limitation ""said disease" or said at least one disease". There is insufficient antecedent basis for this limitation in the claims.

Claims 21-25, 29 and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "full-length AUR1 or AUR2 protein" in claim 21 and its dependent claims is unclear. Applicant all through the specification refers to AUR1-2 as polypeptides. However, in currently amended claims he/she suddenly refers to said polypeptides as "proteins". Applicant is advised to refer to said products in a consistent manner based on the support provided in the specification. **For examination purposes it is assumed that full-length AUR1-2 polypeptides and full-length AUR1-2 proteins are referring to identical products, namely SEQ ID NO:3-4, respectively.**

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21-22, 24-25, 29, 31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (i) method of treating colon and pancreatic cancer by administering to a patient in need of such treatment a substance that modulates the kinase activity of full-length AUR1 and (ii) a method treating colon

cancer by administering to a patient in need of such treatment a substance that modulates the kinase activity of full-length AUR2, does not reasonably provide enablement for methods of treatment of breast cancer, renal cancer, ovarian cancer, bladder cancer, head and neck cancers, melanoma, glioma, medulloblastoma or chondrosarcoma by administering to a patient modulators of kinase activity of full-length AUR1 protein or methods of treatment of breast cancer, renal cancer, ovarian cancer, bladder cancer, head and neck cancers, pancreatic cancer, melanoma, glioma, medulloblastoma or chondrosarcoma by administering to a patient modulators of kinase activity of full-length of AUR2 protein.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2n 1400 (Fed. Cir. 1988) are: 1) the quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breadth of the claims.

In traversal of previous enablement rejection applicant argues that amended claims recite diseases suitable for treatment with Aurora modulators and a clear link has been established between AUR proteins and these disease. According to applicant, Example 2 of the specification demonstrates that AUR1 mRNA is highly expressed in human colon, lung, breast, melanoma and renal cancer cell lines but not in normal adult tissues other than thymus. Said example also shows that AUR2 is highly expressed in colon cancer cell lines and moderately expressed in lung cancer cell lines.

Applicant further states that Example 7, demonstrates that AUR1 and AUR2 are expressed in 96% of colon, renal, melanoma and breast human tumor cell lines. Thus, in applicant's view the application and claims clearly specify diseases suitable for treatment with AUR protein modulators.

Applicant then goes on to refer to Example 10 wherein rat fibroblasts expressing AUR2 formed colonies whereas cells expressing a kinase inactive AUR2 did not do so. Applicant further confirms the growth conferring property of AUR2 be referring to Example 11, wherein transected NIH3T3 cells continue to grow in unfavorable low serum conditions, without anchorage to the support.

Applicant finally refers to anitsense molecules used in Example 12, which downregulated AUR2 expression in human tumor cell line H1299 leading to apoptosis of said tumor cells.

Finally, applicant asserts that said examples contribute strong evidence that skilled artisan can practice claimed methods for treating human cancer by administering Aurora modulator to their afflicted patient.

These arguments were fully considered but again were found **unpersuasive**. The examiner respectfully disagrees with the applicant that a clear link between AUR proteins and claimed diseases, except for the ones indicates above (i.e. colon cancer and pancreatic cancer) has been established by the applicant. With respect to comments directed to examples 2, 7 and 10 above, it should be noted that here, applicant only refers to expression pattern of AUR2 mRNA in a variety of normal and tumor cell lines of human origin. The examiner is unclear how mere expression of

human AUR1 or AUR2 mRNA can be indicator of cancer. This confusion arises due to the fact that many normal and healthy human tissues also express said mRNA (applicant is advised to refer to page 61 of the specification wherein AUR2 has been expressed at high levels in normal liver and thymus cell lines). Hence, it appears that a mere presence of AUR1 or AUR2 mRNA in a tissue, in the absence of control experiment and other supporting evidence, cannot be used as an indicator of cancer.

With respect to Example 11, it is not clear how growth advantage due to presence of AUR2 can be interpreted as cancer inducing and if such link positively exits, which specific cancer claimed are associated with the results of said transfected NIH3T3 cells of Example 11.

In response to comments provided about Example 12, the examiner agrees that antisense molecules may successfully treat some of the cancers claimed (see claim 21), however, as mentioned above, method of use of said molecules are beyond the scope of the instantly elected invention.

In conclusion, in view of explanations provided above, in addition to those provided in the previous office action the rejection is maintained.

Since claim 21 is not enabled, its dependent claims, 24-25, 29 and 31 are not enabled either.

Claims 21-22, 24-25, 29 and 31 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

application was filed, had possession of the claimed invention, as stated in the previous office action. Claim 21 (and its dependent claims 22, 24-25, 29 and 31) as recited, is directed to a **genera** of full-length AUR1 or AUR-2 (proteins) polypeptides from any source and species that have not been adequately described in the specification.

The court of Appeals for the Federal Circuit has recently held that such a general definition does not meet the requirements of 35 U.S.C. 112, first paragraph. " A written description of an invention involving chemical genus, like a description of a chemical species, requires a precise definition, such as be structure, formula {or} chemical name, of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.,* 1997 U.S. App. LEXIS 18221, at *23, quoting *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). The court held that " in claims involving chemical materials, generic formulae usually indicate with specificity what generic claims encompass. One skilled in the art can distinguish such a formula fro others and can identify many of the species that the claims encompass. accordingly, such a formula is normally an adequate description of the claimed genus. In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish it from others. One skilled in the art therefore cannot, as one can do with a fully described genus visualize the identity of the members of the genus". Here, applicant is merely referring to AUR 1-2 proteins by function. The specification fails to teach how much structural homology exists among all members of full-length genera of AUR1-2 proteins from all sources and species. Only a **single**

species for each claimed genus is provided which is not adequate written description from the genera as broadly claimed. Claims 22, 24-25, and 29 and 31 remain rejected for depending from a rejected base claim.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maryam Monshipouri whose telephone number is (571) 272-0932. The examiner can normally be reached on 7:00 a.m to 4:30 p.m. except for alternate Mondays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnanthapu Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maryam Monshipouri Ph.D.

Primary Examiner

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